

[Handwritten signature]
PATENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A non-toxic *Pseudomonas* exotoxin A-like chimeric immunogen comprising in sequence: (1) a cell recognition domain of between 10 and 1500 amino acids that binds to a an epithelial cell surface receptor on the apical surface of a mucosal membrane of a mammal; (2) a translocation domain-having an amino acid sequence at least 95% identical to the sequence of *Pseudomonas* exotoxin A (PE) (SEQ ID NO:2) from amino acid position 280 to amino acid position 344 thereof and wherein the domain is capable of effecting translocation to the cytosol of a cell; (3) an epitope presenting domain of between 5 and 350 amino acids in length and consisting essentially of one cysteine-cysteine loop of a pathogen wherein the loop encodes an epitope of [[the]] a pathogen and wherein the epitope is non-native to PE domain Ib; (4) an endoplasmic reticulum (ER) retention domain wherein the ER domain is capable of effecting translocation to the endoplasmic reticulum of the cell and wherein the ER retention domain lacks ADP ribosylation activity.

Claim 2 (previously presented): The immunogen of claim 1, wherein the cell recognition domain is domain Ia of PE and the translocation domain is domain II of PE.

Claim 3 (previously presented): The immunogen of claim 1 wherein the cell recognition domain is domain Ia of PE.

~~Claim 4 (withdrawn): The immunogen of claim 1 wherein cell recognition domain binds to $\alpha 2$ -macroglobulin receptor (" $\alpha 2$ -MR"), epidermal growth factor ("EGF") receptor; the IL-2 receptor; the IL-6 receptor, HIV-infected cells; a chemokine receptor; a leukocyte cell surface receptor; a ligand for the IgA receptor; or an antibody or antibody fragment directed to a receptor.~~

~~Claim 5 (withdrawn): The immunogen of claim 1 wherein cell recognition domain comprises amino acid sequences of a growth factor or an antibody.~~

Claim 6 (canceled).

Claim 7 (previously presented): The immunogen of claim 1 wherein the translocation domain comprises the amino acid sequence of SEQ ID NO:2, from the amino acid at position 280 to the amino acid at position 364.

Claim 8 (previously presented): The immunogen of claim 1 wherein the translocation domain is domain II of PE.

Claims 9-10 (canceled).

~~Claim 11 (withdrawn): The immunogen of claim 1 wherein the non-native epitope domain comprises an amino acid sequence selected from CTRPNYNKRK RIHIGPGRAY TTKNIIGTIRQAHC (SEQ ID NO:3) or CTRPSNNTRT SITIGPGQBF YRTGDIIGDIRKAYC (SEQ ID NO:4)~~

Claim 12 (previously presented): The immunogen of claim 1 wherein the ER retention domain is domain III of PE having a deletion which eliminates ADP ribosylation activity.

Claim 13 (previously presented): The immunogen of claim 1 wherein the ER retention sequence comprises REDLK (SEQ ID NO:11).

~~Claim 14 (withdrawn): The immunogen of claim 1 which has an amino acid sequence selected from:~~

~~PE (SEQ ID NO:2) except that amino acids 361-384 are substituted with the amino acid sequence: Gly Ala Ala Asn Leu His Cys Gly Ile His Ile Gly Pro Gly Arg Ala Phe Tyr Thr Thr Lys Cys Met Gln Gly Pro Ala Asp (SEQ ID NO:7) and amino acid Glu at position 553 is deleted (ntPE-V3MN14), and~~

~~PE (SEQ ID NO:2) except that amino acids 361-384 are substituted with the amino acid sequence: Gly Ala Ala Asn Leu His Cys Asn Tyr Asn Lys Arg Lys Arg Ile His Ile Gly Pro Gly Arg Ala Phe Tyr Thr Thr Lys Asn Ile Ile Gly Thr Ile Cys Met Gln Gly Pro Ala Asp (SEQ ID NO:8) and amino acid Glu at position 553 is deleted (ntPE-V3MN26).~~

~~Claim 15 (withdrawn): The immunogen of claim 1 wherein the non-native epitope is an epitope from a viral, bacterial or parasitic protozoan pathogen.~~

~~Claim 16 (withdrawn): The immunogen of claim 9 wherein the non-native epitope is an epitope of a V3 loop of gp120 of HIV-1.~~

~~Claim 17 (withdrawn): The immunogen of claim 9 wherein the non-native epitope is an epitope of a principal neutralizing loop of a retrovirus.~~

~~Claim 18 (withdrawn): The immunogen of claim 9 wherein the non-native epitope is an epitope of a major neutralizing loop of HIV-2 or a V3 loop of gp120 of HIV-1 of at least 8 amino acids including a V3 loop apex.~~

Claims 19 to 46 (canceled).

Claim 47 (previously presented): The immunogen of claim 1, wherein the translocation domain comprises ~~an~~ amino acid sequence at least 98% identical to the PE amino acid sequence (SEQ ID NO:2) from amino acid position 280 to amino acid position 344 thereof.

Claim 48 (previously presented): The immunogen of claim 1, wherein the translocation domain comprises ~~an~~ amino acid sequence identical to the PE amino acid sequence (SEQ ID NO:2) from amino acid position 280 to amino acid position 344 thereof.

Claim 49 (previously presented): The immunogen of claim 1, wherein the mammal is a rodent or rabbit.

Claim 50 (previously presented): The immunogen of claim 1, wherein the mammal is a primate or a human.

Claim 51 (previously presented): The immunogen of claim 1, wherein the translocation domain comprises an amino acid sequence consisting essentially of the PE amino acid sequence (SEQ ID NO:2) from amino acid position 280 to amino acid position 344 thereof.

Claims 52 to 54 (canceled),

Claim 55-(currently amended): The immunogen of claim 1, wherein the cysteine-cysteine loop of the pathogen is located within domain Ib of [[p]]Pseudomonas exotoxin A in place of amino acid residues 372 to 379, inclusive, of SEQ ID NO:2.

Claim 56 (currently amended): A non-toxic *Pseudomonas* exotoxin A-like chimeric immunogen comprising in sequence: (1) a cell recognition domain of between 10 and 1500 amino acids that binds to a cell surface receptor of a cell from a mammal; (2) a translocation domain having an amino acid sequence at least 95% identical to the sequence of *Pseudomonas* exotoxin A (PE) (SEQ ID NO:2) from amino acid position 280 to amino acid position 344 thereof and wherein the domain is capable of effecting translocation to the cytosol of the cell; (3) an epitope presenting domain of between 5 and 350 amino acids in length and consisting essentially of one cysteine-cysteine loop of a pathogen wherein the loop encodes an epitope of [[the]] a pathogen and wherein the epitope is non-native to PE domain Ib and wherein the cysteine-cysteine loop of the pathogen is located within PE domain Ib in place of amino acid residues 372 to 379, inclusive, of SEQ ID NO:2; (4) an endoplasmic reticulum (ER) retention domain wherein the ER domain is capable of effecting translocation to the endoplasmic reticulum of the cell[[.]].

Claim 57 (previously presented): The immunogen of claim 56, wherein the cell recognition domain is domain 1a of PE and the translocation domain is domain II of PE.

Claim 58 (previously presented): The immunogen of claim 56 wherein the cell recognition domain is domain Ia of PE.

Claim 59 (new): The immunogen of claim 1 wherein the ER retention sequence comprises KDEL (SEQ ID NO:13) or REDL (SEQ ID NO:12).

Claim 60 (new): The immunogen of claim 1, wherein the amino acid sequence of the ER retention domain is 95% identical to the amino acid sequence of SEQ ID NO:2 spanning amino acid positions from 400 to 613 thereof, wherein the ER retention domain has a deletion of the amino acid at position 553 of SEQ ID NO:2 and, optionally, a deletion of the lysine at position 613 of SEQ ID NO:2.

Claim 61 (new): The immunogen of claim 1, wherein the translocation domain comprises the amino acid sequence of SEQ ID NO:2 at position 279 and the amino acid at position 279 is arginine.